10/086 157

~~10/148613~~

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 APR 2004 HIGHEST RN 676591-92-7
DICTIONARY FILE UPDATES: 25 APR 2004 HIGHEST RN 676591-92-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\086157.str

L8 STRUCTURE UPLOADED

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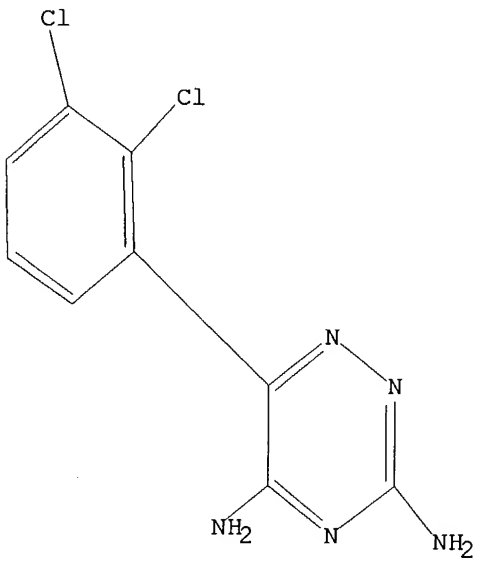
L8 HAS NO ANSWERS
L8 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l8 sss full
FULL SEARCH INITIATED 15:27:41 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 64 TO ITERATE

100.0% PROCESSED 64 ITERATIONS 33 ANSWERS
SEARCH TIME: 00.00.01

~~10/148613~~

L9 33 SEA SSS FUL L8

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	155.84	376.59

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-8.32

FILE 'CAPLUS' ENTERED AT 15:27:51 ON 27 APR 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 27 Apr 2004 VOL 140 ISS 18
FILE LAST UPDATED: 26 Apr 2004 (20040426/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l9
L10 776 L9

=> s l9 and crystalline
776 L9
64329 CRYSTALLINE
190 CRYSTALLINES
64503 CRYSTALLINE
(CRYSTALLINE OR CRYSTALLINES)
313746 CRYST
1798 CRYSTS
315013 CRYST
(CRYST OR CRYSTS)
334154 CRYSTALLINE
(CRYSTALLINE OR CRYST)
L11 2 L9 AND CRYSTALLINE

=> s l9 and solid
776 L9
909769 SOLID
265055 SOLIDS
1105814 SOLID
(SOLID OR SOLIDS)
L12 16 L9 AND SOLID

=> s l9 and solvate

10/~~148613~~

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          776 L9
         8012 SOLVATE
         4019 SOLVATES
        10960 SOLVATE
                (SOLVATE OR SOLVATES)
L13        4 L9 AND SOLVATE

=> d l11 1-2 ibib abs hitstr

L11  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         1996:616102  CAPLUS
DOCUMENT NUMBER:          125:256936
TITLE:                    Moisture-Dependent Crystallization of Amorphous
                          Lamotrigine Mesylate
AUTHOR(S):                Schmitt, E.; Davis, C. W.; Long, S. T.
CORPORATE SOURCE:         Glaxo Wellcome Inc., Research Triangle Park, NC,
                          27709, USA
SOURCE:                   Journal of Pharmaceutical Sciences (1996), 85(11),
                          1215-1219
                          CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER:                American Chemical Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   A com. available computer-controlled vacuum moisture balance was used for
     determining moisture sorption isotherms of freeze-dried and spray-dried
     lamotrigine mesylate and freeze-dried drug product containing mannitol.  The
     presence or absence of desorption hysteresis and the characteristics of
     the weight-vs.-time profile as a sample was exposed to a defined relative
     humidity ramp were sensitive indicators of moisture-induced crystallization
     Combination of the moisture sorption data with polarized light microscopy,
     DSC, and x-ray powder diffraction provided qual. verification of the
     crystallization with <50 mg of sample.  The normalized water loss during
crystallization
     was used to detect as little as 2% amorphous content in phys. mixts. of
     amorphous and cryst. lamotrigine mesylate.  Moisture sorption,
     water plasticization, and crystallization properties of amorphous forms
prepared by
     spray drying and freeze drying were nearly identical.  Cofreeze-drying
     lamotrigine mesylate with D-mannitol resulted in a mixture of amorphous
     lamotrigine mesylate with properties similar to those of spray-dried or
     freeze-dried materials and cryst. D-mannitol.  The amount of water
     needed for crystallization over a time scale observable in the moisture balance
     was considerably more than the amount needed to lower the glass transition
     temperature of the sample to the operating temperature of the instrument.
This result
     illustrated the importance of time scale effects in determining critical
moisture
     levels for crystallization from the amorphous state.
IT   181362-54-9
     RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (moisture-dependent crystallization of amorphous lamotrigine mesylate)
RN   181362-54-9  CAPLUS
CN   1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, methanesulfonate
     (9CI)  (CA INDEX NAME)

     CM   1

     CRN  84057-84-1
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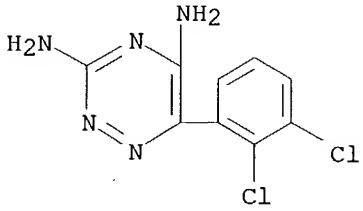
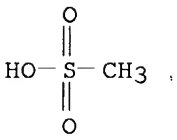


CM 2

CRN 75-75-2
CMF C H4 O3 S



L11 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:464546 CAPLUS
DOCUMENT NUMBER: 125:96152
TITLE: Pharmaceutical granules comprising lamotrigine
INVENTOR(S): Hiskett, Simon Philip; Taylor, Susan Ann
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9617611	A1	19960613	WO 1995-GB2865	19951207
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2207284	AA	19960613	CA 1995-2207284	19951207
AU 9641211	A1	19960626	AU 1996-41211	19951207
AU 696406	B2	19980910		
EP 797441	A1	19971001	EP 1995-939352	19951207
EP 797441	B1	20020227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
CN 1174505	A	19980225	CN 1995-197473	19951207
HU 77367	A2	19980330	HU 1997-2196	19951207
BR 9509975	A	19980609	BR 1995-9975	19951207
JP 10510255	T2	19981006	JP 1995-517420	19951207

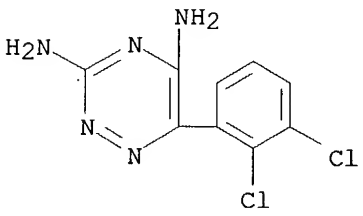
JP 2977284	B2	19991115			
RU 2160106	C2	20001210	RU 1997-111870		19951207
AT 213633	E	20020315	AT 1995-939352		19951207
ES 2172600	T3	20021001	ES 1995-939352		19951207
FI 9702434	A	19970609	FI 1997-2434		19970606
NO 9702623	A	19970806	NO 1997-2623		19970606
US 5861179	A	19990119	US 1997-849070		19970626
PRIORITY APPLN. INFO.:			GB 1994-24766	A	19941207
			WO 1995-GB2865	W	19951207

AB A pharmaceutical formulation comprises: (a) from 0.5 to 50% by weight of lamotrigine or a pharmaceutically acceptable acid addition salt thereof, (b) from 15 to 50% by weight of lactose, (c) from 15 to 50% by weight of starch, (d) from 0.5 to 15% by weight of **cryst**. cellulose, and (e) from 5 to 15% by weight of polyvinylpyrrolidone, and which is in the form of a free-flowing powder of granules having the following properties: (1) no granules have a particle size of greater than 850 μm, (2) at least 90% by weight of the granules have a particle size of from 75 to 850 μm, (3) the granules disintegrate within 30 min according to the Disintegration Test of The Pharmacopoeia of Japan, twelfth edition, 1991, and (i.v.) of at least 90% by weight of the lamotrigine or lamotrigine salt in the granules dissolves within 30 min when the granules are subjected to the dissoln. test, method 2 (paddle method) of the Pharmacopoeia of Japan, twelfth edition, 1991. Formulation of various granules are disclosed.

IT **84057-84-1**, Lamotrigine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical granules comprising lamotrigine)

RN 84057-84-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



=> d l12 1-16 ibib abs hitstr

L12 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2003:875073 CAPLUS
DOCUMENT NUMBER:	139:354488
TITLE:	Pharmaceutical composition containing lamotrigine particles of defined morphology
INVENTOR(S):	Aronhime, Judith; Samburski, Guy
PATENT ASSIGNEE(S):	Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE:	PCT Int. Appl., 24 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003090693	A2	20031106	WO 2003-US13002	20030423
WO 2003090693	A3	20040108		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

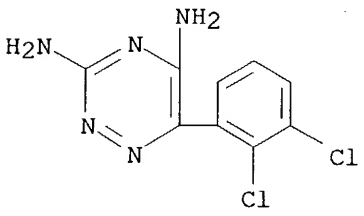
PRIORITY APPLN. INFO.: US 2002-374923P P 20020423

AB The present invention provides a pharmaceutical composition comprising a plurality of lamotrigine particles having a sp. surface area of from about two to about three and a half meters per g. Pharmaceutical compns. falling within the surface area criteria for the lamotrigine particles include those having a particle diameter equal to or less than about 100 μm, preferably about 50 μm, and most preferably 10 μm. The pharmaceutical composition can be formulated into a wide variety of dosage forms for treatment of seizures.

IT **84057-84-1**, Lamotrigine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition containing lamotrigine particles of defined morphol.
and excipients)

RN 84057-84-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



L12 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2003:422192 CAPLUS
DOCUMENT NUMBER:	140:72234
TITLE:	Screening for Basic Drugs in 2-mL Urine Samples by Dual-Plate Overpressured Layer Chromatography and Comparison with Gas Chromatography-Mass Spectrometry
AUTHOR(S):	Pelander, Anna; Ojanperae, Ilkka; Sistonen, Johanna; Rasanen, Ilpo; Vuori, Erkki
CORPORATE SOURCE:	Department of Forensic Medicine, University of Helsinki, FIN-00014, Finland
SOURCE:	Journal of Analytical Toxicology (2003), 27(4), 226-232 CODEN: JATOD3; ISSN: 0146-4760
PUBLISHER:	Preston Publications
DOCUMENT TYPE:	Journal
LANGUAGE:	English

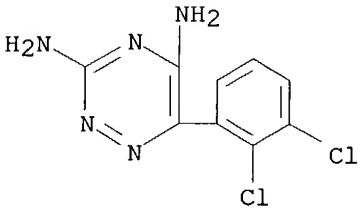
AB A dual-plate overpressured layer chromatog. (OPLC) method was evaluated for broad-scale screening of basic drugs in 2-mL autopsy urine samples.

Extraction was carried out by mixed-mode **solid**-phase extraction, and identification was based on automated comparison of corrected Rf values (hRfc) and in situ UV spectra with library values by dedicated software. The day-to-day precision of hRfc values was good in both OPLC1 and OPLC2 systems with median relative standard deviations of 2.4% and 3.4%, resp. Both Rf and hRfc values were independent of the amount of analyte (0.5-10 μg) applied to the plate. Detection limits were determined for 47 drug substances in 2-mL urine samples, and they varied between 0.05 and 3.5 mg/L with a median of 1.0 mg/L. The performance of OPLC was evaluated by analyzing 30 autopsy urine samples by both OPLC and gas chromatog.-mass spectrometry (GC-MS). The majority of findings by OPLC were in agreement with GC-MS. Some substances with low concns. were not detected by OPLC, whereas GC-MS failed to detect a few polar substances. The OPLC method thus provides an alternative for current planar and column liquid chromatog. drug screening methods with the possibility of lowering detection limits by using a larger sample size. (c) 2003 Preston Publications.

IT **84057-84-1,** Lamotrigine
RL: ANT (Analyte); ANST (Analytical study)
(forensic screening for basic drugs in 2-mL urine samples by dual-plate overpressured layer chromatog. and comparison with gas chromatog.-mass spectrometry)

RN 84057-84-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:291183 CAPLUS

DOCUMENT NUMBER: 139:202670

TITLE: Microemulsion electrokinetic chromatography applied for separation of levetiracetam from other antiepileptic drugs in polypharmacy

AUTHOR(S): Ivanova, Mariela; Piunti, Alessandra; Marziali, Ettore; Komarova, Natalja; Raggi, Maria Augusta; Kenndler, Ernst

CORPORATE SOURCE: Institute for Analytical Chemistry, University of Vienna, Vienna, A-1090, Austria

SOURCE: Electrophoresis (2003), 24(6), 992-998
CODEN: ELCTDN; ISSN: 0173-0835

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal

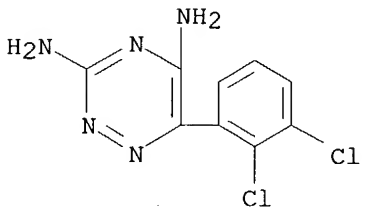
LANGUAGE: English

AB Microemulsion electrokinetic chromatog. was applied for the separation of levetiracetam from other antiepileptic drugs (primidone, phenobarbital, phenytoin, lamotrigine, and carbamazepine) that are potentially coadministered in therapy of patients. The influence of the composition of the microemulsion system (with sodium dodecyl sulfate as charged surfactant) was investigated, modifying the kind of cosurfactant (lower alcs. from C3 to C5), the pH (and salinity) of the aqueous background electrolyte, and the

ratio of aqueous phase to organic constituents forming the microdroplets of the oil-in-water emulsion. Separation selectivity was depending on all these parameters, resulting even in changes of the migration sequence of the analytes. Only moderate correlation was observed for the microemulsion system compared with a micellar system, both consisting of the aqueous borate buffer (pH 9.2) and SDS as micelle former (linear correlation coefficient for analyte mobilities is 0.974). The sample solvent plays an important role on the shape of the resulting chromatograms: MeOH at concns. higher than 35% impairs peak shape and separation efficiency. The microemulsion method (with 93.76% aqueous borate buffer (pH 9.2, 10 mM), 0.48% n-octane, 1.80% SDS, 3.96% 1-butanol, all weight/weight) is suitable for the determination of levetiracetam in human plasma (combined with a sample pretreatment based on **solid**-phase extraction).

IT **84057-84-1**, Lamotrigine
RL: ANT (Analyte); ANST (Analytical study)
(microemulsion electrokinetic chromatog. applied for separation of levetiracetam from other antiepileptic drugs in polypharmacy)

RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:154224 CAPLUS
DOCUMENT NUMBER: 138:193294
TITLE: Expandable gastric retention device containing pharmaceutical compositions
INVENTOR(S): Ayres, James W.
PATENT ASSIGNEE(S): The State of Oregon Acting by and Through the State Board of Higher Education On Behalf of Oregon State University, USA
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015745	A1	20030227	WO 2001-US46146	20011022

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

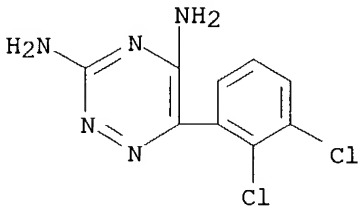
PRIORITY APPLN. INFO.: US 2001-313078P P 20010816

AB The present application concerns gastric retention devices formed from compns. comprising polymeric materials, such as polysaccharides, and optional addnl. materials including excipients, therapeutics, and diagnostics, that reside in the stomach for a controlled and prolonged period of time. Dry powders of xanthan gum and locust bean gum were mixed intimately were converted to dried films. The dried films were compressed with the help of specially made punches and dies. A series of dies with decreasingly narrow internal diams. were used. A punch pushes the film from one die into the next die, followed by pushing of the film by another punch into the next die. This process takes place in succession until a point is reached where the film is small enough to put into a desired capsule size.

IT **84057-84-1**, Lamotrigine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(expandable gastric retention device containing pharmaceutical compns.)

RN 84057-84-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:831233 CAPLUS

DOCUMENT NUMBER: 138:362055

TITLE: Simultaneous analysis of six antiepileptic drugs and two selected metabolites in human plasma by liquid chromatography after **solid**-phase extraction

AUTHOR(S): Bugamelli, F.; Sabbioni, C.; Mandrioli, R.; Kenndler, E.; Albani, F.; Raggi, M. A.

CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Bologna, Bologna, 40126, Italy

SOURCE: Analytica Chimica Acta (2002), 472(1-2), 1-10
CODEN: ACACAM; ISSN: 0003-2670

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

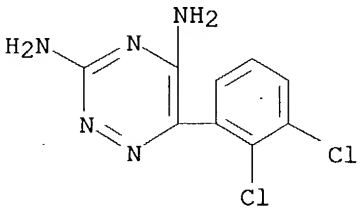
LANGUAGE: English

AB A rapid and simple liquid chromatog. method with photodiode array detection was developed for the simultaneous determination of 6 antiepileptic drugs (oxcarbazepine, carbamazepine, Lamotrigine, phenobarbital, primidone, and phenytoin) and 2 metabolites (10,11-dihydro-10,11-epoxycarbamazepine and 10,11-dihydro-10-hydroxycarbamazepine, the main active metabolites of carbamazepine and oxcarbazepine, resp.) in human plasma. Separation of the analytes was achieved in <11.5 min on a C18 column (150+4.0 mm, i.d. 4.5 μm) with a mobile phase composed of methanol, acetonitrile, and a pH 3.0, 15 mM phosphate buffer containing 0.63% triethylamine [19.2:16.8:64.0, (volume/volume/volume)], at 1 mL min-1 flow rate. Two procedures were tested for the pretreatment of human plasma samples: protein precipitation with

perchloric acid and **solid**-phase extraction The protein precipitation procedure did not allow for the anal. of 10,11-dihydro-10,11-epoxycarbamazepine. On the contrary, **solid**-phase extraction with hydrophilic-lipophilic balance cartridges gave good results in terms of extraction efficiency and reproducibility and allowed for the determination of all analytes. The HPLC-DAD method developed, coupled to a careful SPE procedure, seems to be suitable for the plasma level determination of simultaneously administered antiepileptic drugs.

IT **84057-84-1**, Lamotrigine
RL: ANT (Analyte); ANST (Analytical study)
(simultaneous anal. of antiepileptic drugs and selected metabolites in human plasma by HPLC with diode array detection after **solid**-phase extraction)

RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:676002 CAPLUS
DOCUMENT NUMBER: 137:222039
TITLE: New crystal forms of lamotrigine and processes for their preparations
INVENTOR(S): Garti, Nissim; Berkovich, Yana; Dolitzky, Ben-Zion; Aronhime, Judith; Singer, Claude; Lieberman, Anita; Gershon, Neomi
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002068398	A1	20020906	WO 2002-US6160	20020227
WO 2002068398	C2	20021121		

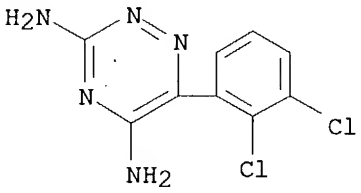
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2003018030 A1 20030123 US 2002-86157 20020227
EP 1390355 A2 20040225 EP 2002-706471 20020227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: US 2001-271688P P 20010227
WO 2002-US6160 W 20020227

AB The present invention relates to lamotrigine, a useful agent for anti-epilepsia. New crystal forms of lamotrigine-containing mols. of the solvent in stoichiometric ratios are disclosed. Processes for preparing the new crystal forms of lamotrigine and dosage forms are also provided. For example, 2 g of lamotrigine anhydrous and about 80 mL of ethanol were charged in a three-necked bottomed round flask equipped with a mech. stirrer, a condenser and a thermometer. The suspension was stirred for about 24 h without heating at about 25° and the **solid** phase was separated by filtration, producing lamotrigine Form H, i.e., lamotrigine ethanol monosolvate.

IT **375347-20-9**, Lamotrigine hydrate **454695-00-2**
RL: CPS (Chemical process); FMU (Formation, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); USES (Uses)
(preparation of crystal forms of lamotrigine as antiepileptic)

RN 375347-20-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, monohydrate (9CI) (CA INDEX NAME)

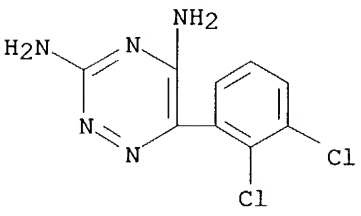


● H_2O

RN 454695-00-2 CAPLUS
CN 2-Propanone, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (9CI) (CA INDEX NAME)

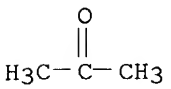
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5

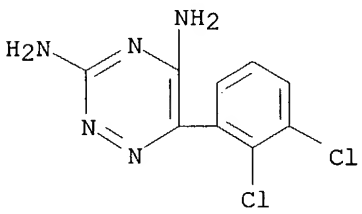


CM 2

CRN 67-64-1
CMF C3 H6 O



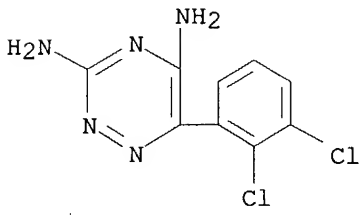
IT **84057-84-1**, Lamotrigine
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of crystal forms of lamotrigine as antiepileptic)
RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



IT **454695-02-4 454695-03-5 454695-04-6**
454695-05-7 454695-06-8 454695-07-9
454695-08-0 454695-09-1 454695-10-4
454695-11-5 454695-12-6 454695-13-7
454695-15-9
RL: FMU (Formation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(preparation of crystal forms of lamotrigine as antiepileptic)
RN 454695-02-4 CAPLUS
CN Formamide, N,N-dimethyl-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

~~10/148613~~

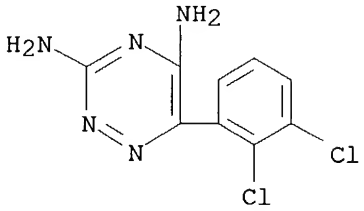
CM 2

CRN 1634-04-4
CMF C5 H12 O

t-Bu—O—Me

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:335789 CAPLUS
DOCUMENT NUMBER: 137:27757
TITLE: Determination of lamotrigine simultaneously with carbamazepine, carbamazepine epoxide, phenytoin, phenobarbital, and primidone in human plasma by SPME-GC-TSD
AUTHOR(S): Queiroz, M. E. C.; Silva, S. M.; Carvalho, D.; Lancas, F. M.
CORPORATE SOURCE: Department of Pharmaceutical Science, University of Ribeirao Preto, Ribeirao Preto, Brazil
SOURCE: Journal of Chromatographic Science (2002), 40(4), 219-223
CODEN: JCHSBZ; ISSN: 0021-9665
PUBLISHER: Preston Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A simple and rapid anal. method is presented for the determination of lamotrigine simultaneously with primidone, carbamazepine, carbamazepine epoxide, phenobarbital, and phenytoin in human plasma using **solid**-phase microextn. (SPME) and gas chromatog. with thermionic specific detection. The best conditions for the SPME procedure is established as following: direct extraction on a 65-μm Carbowax-divinylbenzene fiber; 1.0 mL of a sample plasma matrix modified with 15% NaCl and 3 mL of a K phosphate buffer (pH 7.0); extraction temperature at 30°; and stirring at a rate of 2500 rpm for 15 min. The method shows good linearity between 0.05 and 40.0 μg/mL with regression coeffs. ranging between 0.9965 and 0.9995 and a coefficient of variation of the points of the calibration curve <10%. The lowest limit of quantitation for the plasma-studied drugs varies from 0.05 to 0.20 μg/mL, according to the drug. The proposed method is sensitive enough to work into subtherapeutic and therapeutic concns., being that it is applied in pharmacokinetic studies and patient routine therapeutic drug monitoring. (c) 2002 Preston Publications.
IT **84057-84-1**, Lamotrigine
RL: ANT (Analyte); ANST (Analytical study)
(determination of lamotrigine simultaneously with carbamazepine, carbamazepine epoxide, phenytoin, phenobarbital, and primidone in human plasma by SPME-GC-TSD)
RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)

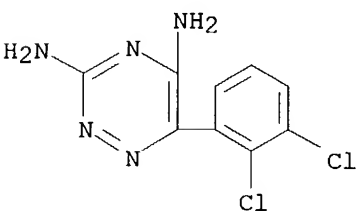


REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:115608 CAPLUS
DOCUMENT NUMBER: 136:226248
TITLE: **Solid**-phase microextraction-liquid chromatography (SPME-LC) determination of lamotrigine simultaneously with carbamazepine and carbamazepine 10,11-epoxide in human plasma
AUTHOR(S): Queiroz, M. E. C.; Silva, S. M.; Carvalho, D.; Lancas, Fernando M.
CORPORATE SOURCE: Department of Pharmaceutical Science, University of Ribeirao Preto, Ribeirao Preto, 14096-380, Brazil
SOURCE: Journal of Separation Science (2002), 25(1/2), 91-95
CODEN: JSSCCJ; ISSN: 1615-9306
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A simple and specific anal. method is presented for the determination of lamotrigine (LTG) simultaneously with carbamazepine (CBZ) and carbamazepine 10,11-epoxide (CBZ-E) in human plasma by off-line **solid**-phase microextn.-liquid chromatog. The best anal. conditions for the SPME procedure were established by direct extraction on a 50 μm Carbowax/TPR-100-coated fiber, employing 1.0 mL of sample plasma matrix modified with 30% NaCl and with 3 mL K phosphate buffer (pH 9.0); extraction at 22°; stirring at a rate of 2500 rpm for 20 min; and then desorption of the drugs by exposure of the fiber to 50 μL of the mobile phase for 10 min. The method showed good linearity (0.05 to 10.0 μg mL-1 for LTG, 0.2 to 20.0 μg mL-1 for CBZ, and 1.0 to 20.0 μg mL-1 for CBZ-E), with regression coeffs. ranging from 0.9947 to 0.9978 and coeffs. of variation of the points of the calibration curve <10%. The limit of quantification (LOQ) for the studied drugs in plasma varied from 0.05 to 1.0 μg mL-1.

IT **84057-84-1**, Lamotrigine
RL: ANT (Analyte); ANST (Analytical study)
(**solid**-phase microextn.-liquid chromatog. (SPME-LC) determination of lamotrigine simultaneously with carbamazepine and carbamazepine 10,11-epoxide in human plasma)
RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:396644 CAPLUS
DOCUMENT NUMBER: 135:24671
TITLE: **Solid** carriers for improved delivery of active ingredients in pharmaceutical compositions
INVENTOR(S): Patel, Manesh V.; Chen, Feng-jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

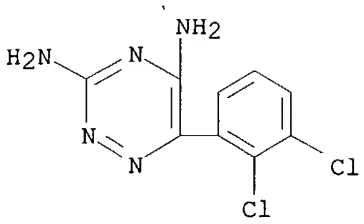
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037808	A1	20010531	WO 2000-US32255	20001122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6248363	B1	20010619	US 1999-447690	19991123
EP 1233756	A1	20020828	EP 2000-980761	20001122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003517470	T2	20030527	JP 2001-539423	20001122

PRIORITY APPLN. INFO.: US 1999-447690 A 19991123
WO 2000-US32255 W 20001122

AB The present invention provides **solid** pharmaceutical compns. for improved delivery of a wide variety of pharmaceutical active ingredients contained therein or sep. administered. In one embodiment, the **solid** pharmaceutical composition includes a **solid** carrier, the **solid** carrier including a substrate and an encapsulation coat on the substrate. The encapsulation coat can include different combinations of pharmaceutical active ingredients, hydrophilic surfactant, lipophilic surfactants and triglycerides. In another embodiment, the **solid** pharmaceutical composition includes a **solid** carrier, the **solid** carrier being formed of different combinations of pharmaceutical active ingredients, hydrophilic surfactants, lipophilic surfactants and triglycerides. The compns. of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritionals, cosmeceuticals and diagnostic agents. A composition contained glyburide 1, PEG 40 stearate 33, glycerol monolaurate 17, and nonpareil seed 80 g.

IT **84057-84-1**, Lamotrigine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**solid** carriers for improved delivery of active ingredients in pharmaceutical compns.)

RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



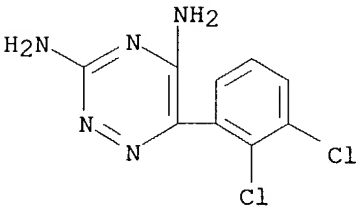
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:516222 CAPLUS
DOCUMENT NUMBER: 131:153391
TITLE: A rapid and sensitive HPLC assay for the determination of lamotrigine in serum
AUTHOR(S): Oertel, Reinhard; Richter, K.; Ebert, U.
CORPORATE SOURCE: Institut Klinische Pharmakologie, Medizinische Fakultat, TU Dresden, Dresden, D-01307, Germany
SOURCE: Pharmazie (1999), 54(8), 628-629
CODEN: PHARAT; ISSN: 0031-7144
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag
DOCUMENT TYPE: Journal
LANGUAGE: German

AB NOTE TO YOU! rifampicin(e) . A rapid, sensitive, and automatic method for determination of lamotrigine in serum was developed. Sample preparation was carried out by **solid**-phase extraction during 12 min per sample. Superspher RP18 end-capped was used for HPLC. Linearity was found between 0.05 and 2 μg/mL. Recoveries of 97.3 and 103.4% were observed at 0.05 and 0.2 μg/mL, resp. Interferences with cimetidine and rifampicin were not observed

IT **84057-84-1**, Lamotrigine
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(HPLC assay for determination of lamotrigine in serum)

RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:311364 CAPLUS
DOCUMENT NUMBER: 130:335011
TITLE: A method for separating non-proteinaceous substances from proteinaceous substances for subsequent processing
INVENTOR(S): Akerman, Satu; Paronen, Petteri; Akerman, Kari;

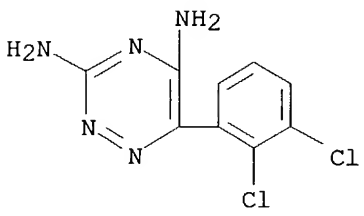
Jarvinen, Kristiina; Kontturi, Kyosti; Nasman, Jan; Svarfvar, Bror; Urtti, Arto; Viinikka, Pasi
PATENT ASSIGNEE(S): Finland
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9923487	A1	19990514	WO 1998-FI852	19981103
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9910342	A1	19990524	AU 1999-10342	19981103

PRIORITY APPLN. INFO.: FI 1997-4124 19971104
WO 1998-FI852 19981103

AB The present invention is directed to a simple but efficient method for separating non-proteinaceous substances, such as drugs and nucleic acids from proteinaceous substances for subsequent monitoring and evaluation. The non-proteinaceous substances are captured by an environmentally sensitive **solid** carrier under physiol. conditions and released under non-physiol. conditions with a solvent, which is compatible with or used in subsequent steps. The **solid** carriers are provided in the form of membranes, sheets, sticks, plates, test tubes, microplates or as beads or granules attached to a further **solid** support. The surface of said carriers are covered with capturing residues, which are sensitive to changes in the environmental conditions, e.g. pH or ionic strength. Said residues are responsible for binding and release of drugs or nucleic acids and allows their easy and rapid separation from proteins. Test kits including said **solid** carriers as well as their applications are also disclosed. Vinylpyridine-grafted poly(vinylidene fluoride) membranes (preparation given) were used to sep. DNA from digest solution
Bound DNA was released with methanol for spectrophotometric anal.

IT **84057-84-1**, Lamotrigine
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(binding of, to grafted polymer membrane; separation of non-proteinaceous substances from proteinaceous substances for subsequent processing)
RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



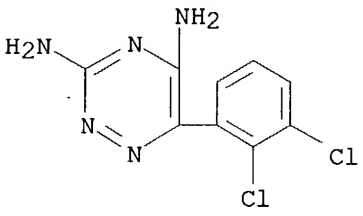
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:196045 CAPLUS
DOCUMENT NUMBER: 129:74
TITLE: Determination of drugs in biological fluids by high-performance liquid chromatography with online sample processing
AUTHOR(S): Oertel, R.; Richter, K.; Gramatte, T.; Kirch, W.
CORPORATE SOURCE: Medical Faculty Carl Gustav Carus, Institute of Clinical Pharmacology, Technical University Dresden, Dresden, D-01307, Germany
SOURCE: Journal of Chromatography, A (1998), 797(1 + 2), 203-209
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An automated two column HPLC system with the new packing material LiChrospher RP-18 ADS (alkyl-diol-silica) was tested for the determination of several drugs and metabolites (talinolol, celiprolol, metoprolol, oxprenolol, triamterene, trimethoprim, tiracizine, articaine, detajmium, ajmaline, lamotrigine) in various biol. fluids (serum, urine, intestinal aspirates, supernatants of cell cultures and supernatants after protein denaturation). The method allows the direct injection of biol. fluids into a reversed-phase HPLC system and online clean-up and sample enrichment by a column-switching technique. Precision, accuracy and sensitivity were similar to conventional assays as described in the literature. With this new method it was possible to measure drug concns. in various biol. fluids without changing the sample preparation procedure. In some cases an addnl. sample preparation like protein denaturation or **solid**-phase extraction was advantageous to enhance the sensitivity of the method and the life-time of the ADS column.

IT **84057-84-1**, Lamotrigine
RL: ANT (Analyte); ANST (Analytical study)
(determination of drugs in biol. fluids by high-performance liquid chromatog.
with online sample processing)
RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

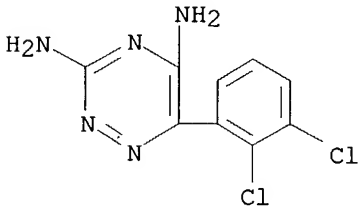
L12 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:627817 CAPLUS
DOCUMENT NUMBER: 127:287584
TITLE: Optimized high-performance liquid chromatographic method for determination of lamotrigine in serum with concomitant determination of phenytoin, carbamazepine,

and carbamazepine epoxide
AUTHOR(S): Lensmeyer, Gary L.; Gidal, Barry E.; Wiebe, Donald A.
CORPORATE SOURCE: Clinical Toxicology Laboratory, Departments of Pathology and Laboratory Medicine and School of Pharmacy, University of Wisconsin Hospital and Clinics, Madison, WI, 53792, USA
SOURCE: Therapeutic Drug Monitoring (1997), 19(3), 292-300
CODEN: TDMODV; ISSN: 0163-4356
PUBLISHER: Lippincott-Raven
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lamotrigine (LG), phenytoin (PY), carbamazepine (CM), and carbamazepine epoxide (CE) are measured with an optimized procedure that uses thin sorbent extraction disks and a highly selective, sterically protected bonded silica high-performance liquid chromatog. (HPLC) column. Routinely, serum (200 μl at pH 6.8 with cyheptamide as internal standard) is applied to an Empore octyl (C8) **solid**-phase extraction disk to isolate the drugs. A water wash removes interferences, and the retained drugs are eluted with a small volume of solvent. The eluate is directly injected into a Zorbax Stable Bond cyanopropyl HPLC column with quantification at 214 nm. Evaporation-concentration steps are unnecessary. Overall, for all drugs, between-run precision coeffs. of variation (each) ranged from 2.1% to 4.9% at concns. from 0.75 to 20.5 mg/l; extraction recoveries fell within a range of 96% to 110% at concns. of 2, 10, and 30 mg/l tested for each drug; the lowest limit of detection was 0.15 to 0.35 mg/l. The anal. response was linear for each drug >80 mg/l (LG) and >50 mg/l (PY, CM, and CE). Optimization graphs are presented to illustrate the rationale for selection of test parameters for a robust method. In addition, a comparison study between two com. labs. demonstrates accuracy problems associated with LG testing.

IT **84057-84-1**, Lamotrigine
RL: ANT (Analyte); ANST (Analytical study)
(determination of lamotrigine in serum with concomitant determination of phenytoin, carbamazepine, and carbamazepine epoxide by HPLC)

RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



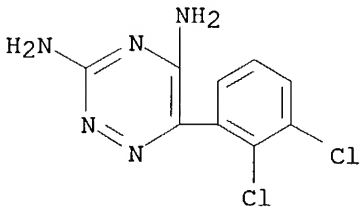
L12 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:671783 CAPLUS
DOCUMENT NUMBER: 125:316089
TITLE: Therapeutic drug monitoring by HPLC gradient separation (MTSS) after fractionated **solid**-phase extraction on a mixed phase
AUTHOR(S): Interschick, Elmar; Rehorek, Astrid; Patscheke, Heinrich; Becker, Wolfgang
CORPORATE SOURCE: Staedt. Klinikum Karlsruhe Klinische Chemie, Karlsruhe, D-76133, Germany
SOURCE: LaborMedizin (1996), 19(4), 150-153

CODEN: LAMEET; ISSN: 0170-205X
PUBLISHER: GIT Verlag
DOCUMENT TYPE: Journal
LANGUAGE: German

AB An anal. procedure is described for the monitoring of seldom-used drugs in serum; it is generally suitable for serum concns. of 20-5000 ng/mL. Basic substances are separated from acidic and neutral drugs by fractionated **solid**-phase extraction on a mixed phase (C8 phase and cation exchanger) during sample preparation Due to the high capacity of the tentacle ion exchanger, the usual pH conversion of the **solid** phase prior to extraction becomes unnecessary. In general, the recovery rates are around 100% and the variation coeffs. are <5%. The chromatog. anal. is carried out by HPLC using a C18 phase low in OH groups which is generally suitable for basic, acidic and neutral components. By means of gradient separation it is possible to detect drugs of different polarities in the same run.

IT **84057-84-1**, Lamotrigine
RL: ANT (Analyte); ANST (Analytical study)
(therapeutic drug monitoring by HPLC gradient separation after fractionated **solid**-phase extraction on a mixed phase)

RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



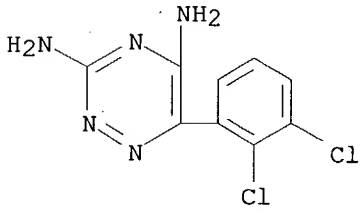
L12 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:778475 CAPLUS
DOCUMENT NUMBER: 123:187597
TITLE: Simple and rapid analysis of lamotrigine, a novel antiepileptic, in human serum by high-performance liquid chromatography using a **solid**-phase extraction technique
AUTHOR(S): Yamashita, Syoichi; Furuno, Katsushi; Kawasaki, Hiromu; Gomita, Yutaka; Yoshinaga, Harumi; Yamatogi, Yasuko; Ohtahara, Shunsuke
CORPORATE SOURCE: Department of Hospital Pharmacy, Okayama University Medical School, 2-5-1 Shikata-cho, Okayama, 700, Japan
SOURCE: Journal of Chromatography, B: Biomedical Applications (1995), 670(2), 354-7
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A simple and rapid method for the quantitation of concns. of lamotrigine, a novel antiepileptic, in human serum was developed with high-performance liquid chromatog., using a **solid**-phase extraction technique. The mobile phase was composed of acetonitrile-10 mM phosphate buffer (pH 3.5) containing 5 mM sodium octanesulfonate (27:73, volume/volume), and components were detected at 265 nm. Retention times of acetanilide as an internal standard and lamotrigine were 3.4 and 10.3 min, resp. The coeffs. of variation were 3.1-4.5% and 4.4-9.8% for the within-day and between-day precision

ests., resp. The extraction recovery of lamotrigine added to blank serum was 86-107%. The quantitation limit of lamotrigine was .apprx.0.2 μg/mL in 100 μl of serum. These results suggest that the method employed in this study is useful for the routine monitoring of serum concns. of lamotrigine in epileptic patients.

IT **84057-84-1**, Lamotrigine
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(simple and rapid anal. of lamotrigine, a novel antiepileptic, in human serum by high-performance liquid chromatog. using a **solid**-phase extraction technique)

RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)

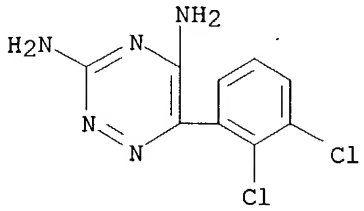


L12 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:774091 CAPLUS
DOCUMENT NUMBER: 123:179633
TITLE: **Solid**-phase extraction study and RP-HPLC analysis of lamotrigine in human biological fluids and in antiepileptic tablet formulations
AUTHOR(S): Papadoyannis, I. N.; Zotou, A. C.; Samanidou, V. F.
CORPORATE SOURCE: Laboratory of Analytical Chemistry, Aristotle Univ., Thessaloniki, GR-54006, Greece
SOURCE: Journal of Liquid Chromatography (1995), 18(13), 2593-609
CODEN: JLCHD8; ISSN: 0148-3919
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An efficient off-line **solid**-phase extraction (SPE) of lamotrigine (LTG), a new antiepileptic drug, from human serum and urine, prior to HPLC anal., was tested and optimized. High extraction recoveries were achieved from C8 bond Elut cartridges (200mg/3ml), using acidic acetonitrile for the elution of LTG and the internal standard, 3,5-diamino-6-(2-methoxyphenyl)-1,2,4-triazine. Isocratic reversed-phase HPLC (RP-HPLC) anal. on octyl silica, using a Lichrosorb RP-8, 5 μm, 250 + 4.6 mm column and a mobile phase consisting of pH 5.6 0.05M acetate buffer-MeCN (72:28) was sensitive and rapid. The identification of LTG was performed by UV detection at 306nm. The method detected approx. 0.9 ng LTG on-column, using a 20-μL loop, and linearity holds from approx. 0.044 to 7.8 μg/mL in standard solns. In plasma and urine, the limits of detection are 1.1 and 1.2 ng, resp., while linearity holds from approx. 0.087 to 3.49 μg/mL. The proposed method was also used for the direct anal. of antiepileptic tablets.

IT **84057-84-1**, Lamotrigine
RL: ANT (Analyte); ANST (Analytical study)
(**solid**-phase extraction HPLC determination of lamotrigine in human biol. fluids and tablets)

RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



=> d l13 1-4 ibib abs hitstr

L13 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:676002 CAPLUS
DOCUMENT NUMBER: 137:222039
TITLE: New crystal forms of lamotrigine and processes for their preparations
INVENTOR(S): Garti, Nissim; Berkovich, Yana; Dolitzky, Ben-Zion; Aronhime, Judith; Singer, Claude; Lieberman, Anita; Gershon, Neomi
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002068398	A1	20020906	WO 2002-US6160	20020227
WO 2002068398	C2	20021121		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003018030	A1	20030123	US 2002-86157	20020227
EP 1390355	A2	20040225	EP 2002-706471	20020227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

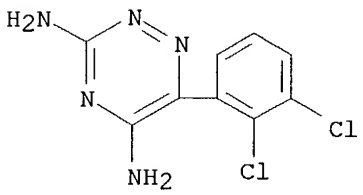
PRIORITY APPLN. INFO.: US 2001-271688P P 20010227
WO 2002-US6160 W 20020227

AB The present invention relates to lamotrigine, a useful agent for anti-epilepsia. New crystal forms of lamotrigine-containing mols. of the solvent in stoichiometric ratios are disclosed. Processes for preparing the new crystal forms of lamotrigine and dosage forms are also provided. For example, 2 g of lamotrigine anhydrous and about 80 mL of ethanol were charged in a three-necked bottomed round flask equipped with a mech. stirrer, a

condenser and a thermometer. The suspension was stirred for about 24 h without heating at about 25° and the solid phase was separated by filtration, producing lamotrigine Form H, i.e., lamotrigine ethanol monosolvate.

IT **375347-20-9**, Lamotrigine hydrate **454695-00-2**
RL: CPS (Chemical process); FMU (Formation, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); USES (Uses)
(preparation of crystal forms of lamotrigine as antiepileptic)

RN 375347-20-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, monohydrate (9CI) (CA INDEX NAME)

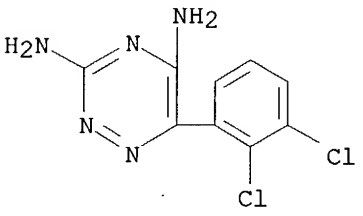


● H_2O

RN 454695-00-2 CAPLUS
CN 2-Propanone, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (9CI) (CA INDEX NAME)

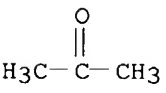
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



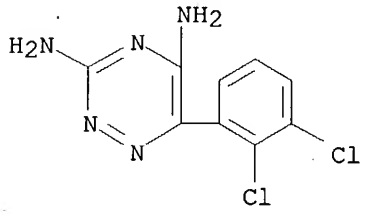
CM 2

CRN 67-64-1
CMF C3 H6 O



IT **84057-84-1**, Lamotrigine

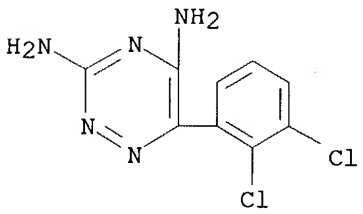
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of crystal forms of lamotrigine as antiepileptic)
RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



IT **454695-02-4 454695-03-5 454695-04-6**
454695-05-7 454695-06-8 454695-07-9
454695-08-0 454695-09-1 454695-10-4
454695-11-5 454695-12-6 454695-13-7
454695-15-9
RL: FMU (Formation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(preparation of crystal forms of lamotrigine as antiepileptic)
RN 454695-02-4 CAPLUS
CN Formamide, N,N-dimethyl-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

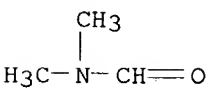
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

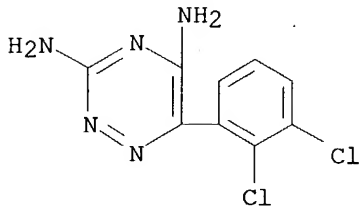
CRN 68-12-2
CMF C3 H7 N O



RN 454695-03-5 CAPLUS
CN 2-Propanol, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (9CI) (CA INDEX NAME)

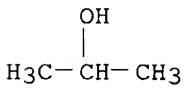
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

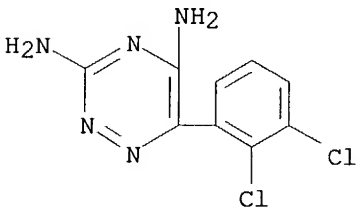
CRN 67-63-0
CMF C3 H8 O



RN 454695-04-6 CAPLUS
CN Formamide, N,N-dimethyl-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (3:2) (9CI) (CA INDEX NAME)

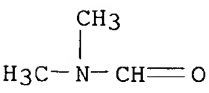
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 68-12-2
CMF C3 H7 N O

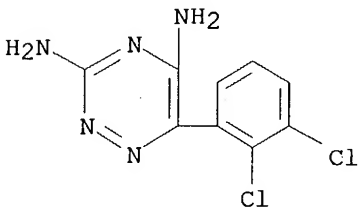


RN 454695-05-7 CAPLUS

CN Formamide, N,N-dimethyl-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (2:3) (9CI) (CA INDEX NAME)

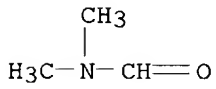
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

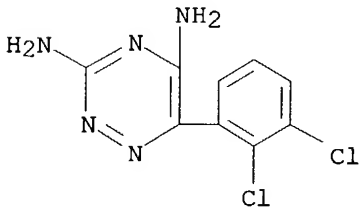
CRN 68-12-2
CMF C3 H7 N O



RN 454695-06-8 CAPLUS
CN Methanol, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (2:3) (9CI) (CA INDEX NAME)

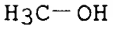
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 67-56-1
CMF C H4 O



RN 454695-07-9 CAPLUS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:472472 CAPLUS
DOCUMENT NUMBER: 135:81972
TITLE: Formulations of adenosine A1 agonists
INVENTOR(S): Bountra, Charanjit; Clayton, Nicholas Maughan; Naylor, Alan
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045684	A2	20010628	WO 2000-GB4888	20001219
WO 2001045684	A3	20020314		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1239880	A2	20020918	EP 2000-985631	20001219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518042	T2	20030603	JP 2001-546423	20001219
US 2003008842	A1	20030109	US 2002-168196	20020618

PRIORITY APPLN. INFO.: GB 1999-30079 A 19991220
WO 2000-GB4888 W 20001219

AB A method of treating conditions associated with pain and alleviating the symptoms associated with it comprises administering to a mammal an adenosine A1 agonist or a salt or **solvate** and a sodium channel blocker. The present invention also provides pharmaceutical formulations and patient packs comprising the combinations. Thus, (2S,3S,4R,5R)-2-(5-tert-butyl-[1,3,4]oxadiazol-2-yl)-5-[6-(4-chloro-2-fluorophenylamino)purin-9-yl]tetrahydrofuran-3,4-diol was prepared in a series of steps by the reaction of (3aS,4S,6R,6aR)-6-(6-chloropurin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxole-4-carboxylic acid with 2,2-dimethylpropionic acid hydrazide followed by the cyclization of the resulting compound, and subsequent treatment with 4-chloro-2-fluoroaniline and deprotection.

IT **84057-84-1**, Lamotrigine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulations of adenosine A1 agonists)

RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)

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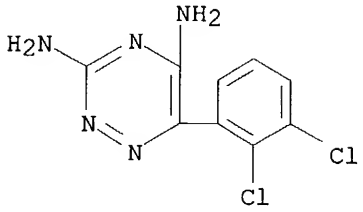


L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:12098 CAPLUS
DOCUMENT NUMBER: 132:130210
TITLE: Structure of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine isethionate **solvate** (lamotrigine isethionate)
AUTHOR(S): Potter, Brian; Palmer, Rex A.; Withnall, Robert; Leach, Michael J.; Chowdhry, Babur Z.
CORPORATE SOURCE: Department of Crystallography, Birkbeck College, University of London, London, WC1E 7HX, UK
SOURCE: Journal of Chemical Crystallography (1999), 29(6), 701-706
CODEN: JCCYEV; ISSN: 1074-1542
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

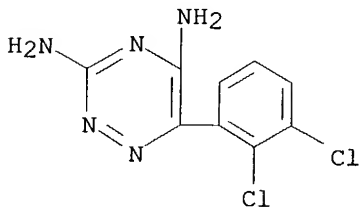
AB The crystal and mol. structure of lamotrigine isethionate was determined by direct methods. The compound crystallizes in the tetragonal space group I41/a, with a 19.684(5), c 16.557(5) Å; Z = 16, dc = 1.579; R = 0.0532, Rw = 0.1317 for 2041 reflections. Atomic coordinates are given. The isethionate moiety forms multiple H bonds to the lamotrigine nucleus, three from one isethionate, two from a symmetry related isethionate and a further two from two different symmetry related mols. Protonation of N(2') in the triazine ring, not observed in the native lamotrigine structure is presumably associated with the interaction of the isethionate moiety. Both rings in the lamotrigine moiety are essentially planar, with a dihedral angle of 66.08(7)° compared to 80.70° in native lamotrigine. The connecting bond length C(1)-C(6') 1.493(3) Å also correlates well with values in related compds. (1.480(3) Å) in the native structures.

IT **113170-86-8**, Lamotrigine isethionate
RL: PRP (Properties)
(crystal structure of)

RN 113170-86-8 CAPLUS
CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



~~10/140613~~

CM 2

CRN 107-36-8
CMF C2 H6 O4 S

HO—CH_2—CH_2—SO_3H

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:126056 CAPLUS
DOCUMENT NUMBER: 110:126056
TITLE: Structure of lamotrigine methanol **solvate**: 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine-methanol, a novel anticonvulsant drug
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LANGUAGE: English

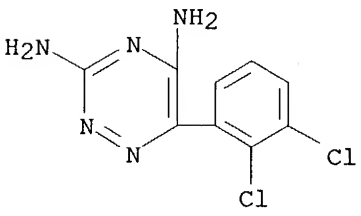
AB The title compound is monoclinic, space group P21/n, with a 15.456(3), b 11.736(2), c 7.300(3) Å, and β 94.417(3)°; Z = 4 for dc = 1.449. The final R = 0.055 for 2444 reflections. Atomic coordinates are given. The Ph and triazine aromatic rings make a dihedral angle of 80.6(9)° with each other. The bond linking the 2 rings is 1.480(3) Å. The structure is stabilized by a network of H bonds involving amino and ring N atoms, one of the Cl atoms, and the MeOH of crystallization

IT **119441-74-6**
RL: PRP (Properties)
(crystal structure of)

RN 119441-74-6 CAPLUS
CN Methanol, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 67-56-1
CMF C H4 O